Cucurbita pepo and Cucurbitacin in the Management of Anti-proliferation by JAK/STAT Pathway

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ABSTRACT

Pumpkin (Cucurbita pepo) is capacious recycled similar to food and in folk medicine throughout the world. It accords to genus Cucurbita (C_CT) under family Cucurbitaceae. There are a plenty of important medicinal phyto-constituents belonging to cucurbitoside like triterpenoids, C_AR, C_CT and glycosides. A survey of the literature demonstrates that C. pepo, has the capacity to improve prostatic hyperplasia, urinary dysfunction and cytotoxic properties. Many pharmacological revisions have established its role in hepatoprotection, inhibition of P_at gland cancer (C_NCR), anti (A^n) oxidant effects, inhibition of L_o, B_p and triple-negative B_p and C_NCR by blocking JAK/STAT signaling (S_tw) pathway (P_rw). It has also A^n microbial, A^n-inflammatory, A^n-diabetic and A^n ulcer activities by supporting its traditional claims. Establishment of C. pepo and cucurbitacin (C_CB) in the management of A^n-proliferation by JAK/STAT P_rw. Data towards writing this review are generated through exploration of different websites like MEDLINE (PubMed), Google Scholar, Science Direct, Scopus, Cochrane, SID and Magiran databases. We have selected 2016-2018 duration for the same purpose. We have found 88 papers related to this topic. C_CB is found to arrest unlimited cell (C_EL) division and respective apoptosis (A_ppt) in vitro and in vivo C_NCR models. A plenty of molecular design targeting C_CB have been invented, such as fibrous-actin, S_ga transducer and activator of transcription (STAT), cyclooxygenase-2, etc. This review is minded at C_CB from C. pepo which dwindle the proliferation of human C_NCR C_EL through the JAK/STAT P_rw.

Key words: Anticancer activity, Cucurbita pepo, Cucurbitaceae family, JAK/STAT pathway, Cucurbitacin, Cyclooxygenase-2.

INTRODUCTION

C_NCR lies its uniqueness to the maximum normally identified diseases (D_SEAS) and is associated with ill health and death set up causing a health problem globally. Even though unlimited determinations have been found ready to find out a remedy, C_NCR remnants a very projecting cause of death in humans. Carcinogenesis (C_CNG) is a different step and different factorial process including the incidence of vibrant and disconnected molecular and C_EL modifications. There are different but thoroughly associated stages of origination, elevation and development are found in C_NCR. Present-day C_NCR treatments, chemotherapy, targeted agents, radiation, surgery and immunosuppression have restrictions subsequent from the expansion of resistance to the treatment. The identification of defensive molecules starved of side effects ruins a crucial independent in the fight against C_NCR. The additional choices goal next to the initial finding of C_NCR in the preliminary stage can assist with its appropriate supervision. In the meantime, plant (P_L)-derived products have taken a major role to inhibit numerous chronic D_SEAS, as well as C_NCR. The use of P_L substances to inhibit or defer the growth of C_CNG has been called for chemoprevention and there is a rapid increasing attention towards the usage of natural compounds as probable chemo-protective and therapeutic.
agents. Pumpkin (P<sub>MPN</sub>) seed (S<sub>Ed</sub>) has several health benefits. P<sub>MPN</sub> is refined all over the biosphere for usage as root vegetables as well as medicine. It is also recycled by tradition as medicine in many nation-states such as China, Yugoslavia, Argentina, India, Mexico, Brazil and America. Its extensively detained medicinal (M<sub>ekl</sub>) usages have concentrated investigation with modern implements and recognized with good A<sup>n</sup> -diabetic, A<sup>n</sup> -hypertension, A<sup>n</sup> -tumor(t<sup>em</sup>), immunomodulation, A<sup>n</sup> bacterial, A<sup>n</sup> -hypercholesterolemia, intestinal A<sup>n</sup> -parasitic, A<sup>n</sup> -inflammatory and analgesic properties.

**Cucurbita pepo**

P<sub>MPN</sub> (*Cucurbita pepo*) is one of the eldest identified nurtured classes of shrub. It accords to the genus C<sub>Ct</sub> and family Cucurbitaceae or C<sub>Ct</sub> and contain crops like cucumbers. Ethno-pharmacological studies display that *C. pepo* is harvested in various countries for treating many D<sub>SEAS</sub> like inflammation, viral infections, pain, urinary disorders, ulcer, diabetes and oxidation. Mainly Ayurveda system has to assess segment of the P<sub>Ed</sub> as well as corpuscles of the fruits (P<sub>r</sub><sup>ct</sup>) and S<sub>Ed</sub>. The S<sub>Ed</sub> are recycled to treat the problems of urinary system, hypertension, kidney stones, prostate (P<sub>r</sub><sup>ut</sup>) D<sub>SEAS</sub>, erysipelas skin (P<sub>r</sub><sup>ek</sup>) infection and carcinomas (C<sub>Arom</sub>). Exact cultivars of winter squash resulting from other species such as *C. argyrosperma* and *C. moschata*, are also at times called “P<sub>MPN</sub>”.

**Taxonomical Classification of *C. pepo***

**Taxonomic classification.**

Kingdom: Plantae

Subkingdom: Tracheobionta

Super division: Spermatophyta

Division: Magnoliopsida

Subclass: Dileniidae

Order: Violales

Family: Cucurbitaceae

Genus: C<sub>Ct</sub> L.

Species: C<sub>Ct</sub> pepo L.

**Vernacular Names**

Hindi: Safed Kaddu, Kumrha Marathi: Kohala, Bhopli Telugu: budadegummadi, Bengali: Safed Kaddu, Sanskrit: karkaru, kurkaru and kurlaru, kushmanda

English: squash.

**Habitat**

P<sub>MPN</sub> are full-fledged throughout the biosphere for a diversity of explanations extending from agronomic ulterior motive. Only Antarctica is not capable to harvest P<sub>MPN</sub>. The major international manufacturers of P<sub>MPN</sub> consist of the United States, Canada, Mexico, India and China.

**Plant Characteristics**

P<sub>MPN</sub> is yearly parsley with heavy mounting stems. The root is thriving established and towards 40 cm unfathomable with 5m extended. The stems are a branch off, enclosed in spongy white up to 10 m long and frequently yield extrinsic roots at nodes. The petioles are 5-20 cm long. The tinny leaves are alternative, modest, palmate, veined, round to reniform, essentially corolate, apically obtuse, unsubdivided to trivial 5-7 lobed, 7-30 cm across, wide-ranging than long, stark to soft blooming and finely margin with toothlike projection, 3-5 rounded or obtuse, apiculate lobules, the central one bigger than lateral ones. Unisexual flowers of P<sub>MPN</sub> are aromatic. The calyx is enclosed in white pubescence and bears 5 free sepals, 0.5-2 cm long. The corolla is yellow to orange color, tubular at least 5 cm long and broad. Staminate flowers are about 10-23 cm long. Pistillate flowers are grown on shorter pedicles, only up to 5.5 cm long and have an inferior 1-ocular ovoid ovary with a short thick style with 3-5 bilobed stigmas. P<sub>r<sup>ut</sup></sub> are highly inconstant in shape, color and size. The shape is elongated, cylindrical, oval, flattened, globular, heart-shaped and tapering to a curved neck on one or both ends. The length is from 5.8 to 71.6 cm and width from 11.2 to 48.6 cm. The S<sub>Ed</sub> can be smooth, wrinkled. The flesh, variable in color and thickness can be white, yellow, or orange and 1 to 6.4 cm thick [Figure 1].

**S<sub>Ed</sub> Characteristics**

P<sub>MPN</sub> S<sub>Ed</sub> is also recognized as pepita. The S<sub>Ed</sub> are characteristically flat, unequally oval, light green in color and typically enclosed by a white husk [Figure 2]. P<sub>MPN</sub> S<sub>Ed</sub> produce 34-54% oil. The size and weight of the S<sub>Ed</sub> rise as the P<sub>r<sup>ct</sup></sub> size rises, lining up between 1.6 to 2.9 cm long, 0.7 to 1.6 cm wide and 0.28 to 0.69 cm thick. The S<sub>Ed</sub> seem doable for 6-8 years but abide by no endosperm and the embryo embody leaf-like cotyledons and a short radicle. P<sub>MPN</sub> S<sub>Ed</sub> oil is popular as succulent oil and also used as a nutritious food. P<sub>MPN</sub> S<sub>Ed</sub> and its oil are prosperous in phytoestrogens, polyunsaturated fatty acids (F<sub>ry</sub>), A<sup>n</sup> -oxidant vitamins, carotenoids (C<sup>Ar</sup>), Tocopherols and its versatile facets such as protein, magnesium, copper and zinc. Due to the presence of these constituents, P<sub>MPN</sub> are recognized as a good reservoir for providing many health remunerations.

**Chemical composition of *C. pepo***

These are categorized through a low contented fat (2.3%), mono-di-poly saccharides (66%), proteinoids substances (3%) and high C<sup>Ar</sup> contented with...
magnitudes of 171.9 to 461.9 microgram. The mineral investigation specified that $P_{MPN}$ pulp is enclosed with great levels of elements which shown in Table 1. The structure of $P_{MPN} S_{Ed}$ is reasonably varying. The content of amino acids ($A^C_d$), $F_{TA}$ and minerals may differ significantly, depending on changed conditions. Such changes may be affected by differences in cultivar or origin. $P_{MPN} S_{Ed}$ contain 50% fatty oil which is dark green and rich in free $F_{TA}$. The arrangement of $F_{TA}$ differs on numerous factors ($F^{CT}$) like the variety of places where the $P_{mp}$ are developed, weather, growth $F^{CT}$ and favoring ripeness. The instabilities in the oil constituents is very high, subsequent from a wide $G^n_a$ variation, farming atmosphere, storage time and storage conditions. The glyceride part content varies from 73.1% to 80.7% unsaturated $F_{TA}$, mainly oleic acid ($OA^C_d$) and linoleic ($L A^C_d$). Again, the same fraction contains 19% saturated $F_{TA}$ consisting of mainly palmitic ($P A^C_d$) and stearic acids ($S A^C_d$) (6%). Several studies have reported similar types of data regarding proportions of total $F_{TA}$ or free $F_{TA}$ in the cake fraction of $P_{MPN} S_{Ed}$: 29.9% $L A^C_d$ and $OA^C_d 50.4%$ [Table 2].

$P_{MPN} S_{Ed}$ are enclosed comparatively huge quantities of $K$ (5,790 $\mu$g/g dry weight) and chromium (approximately 3 $\mu$g/g dry weight). Other minerals present in $P_{MPN} S_{Ed}$ are: P (15,700); Ca (346); iron (106); Mn (49.3); Al (9.21); Ba (1.16); Co (0.29); strontium (1.83); Ni (0.53); As (0.45) (in $\mu$g/g dry weight). Notable is the low amounts of calcium in the $S_{Ed}$. One hundred-gram roasted $P_{MPN} S_{Ed}$ contain 25.94 mg Ca, 955.81 mg P and 8.06 mg of Fe. Numerous constituents such as $C^{AR}_p$, as lutein(1''), 1''-epoxide, 15- cis- L$^a$, 13(13')-cis - L$^a$, $\alpha$ - $C^{AR}_p$ $\beta$ - $C^{AR}_p$, violaxanthin(X$^n$), auro X$^n$ epimers, flavo X$^n$, lute X$^n$, chrysanthema X$^n$ , $\beta$-crypto X$^n$, are also present. Acylated phenolic glycosides ($G^a$) such as cucurbitoside F, H, I, K, L, M, 23-24- dihydroy C$^{CBT}_R$, lariiresinol ($L^{CR}_S$), seco-iso $L^{CR}_S$, iso $L^{CR}_S$, l$^{CR}_S$ -4' -$\beta$- D- G$^{\alpha_o}$, l$^{CR}_S$ - 4-o-$\beta$- beta-d G$^{\alpha_o}$, (24s)-stigmata- 7,22E, 25-trien- 3-one, (24s)-stigmasta-7,22 E, 25-trien-3beta-ol, C$^{CBT}_R$ L.2-O-$\beta$-D-glucopyranoside. Others Phytostartains are also exhibited in Table 3.

### Anti- C$^{NCR}_o$ Mechanism of C. pepo

C$^{NCR}_o$ is the deregulation product of programmed $C^{EL}_o$ death. Numerous favorable goals for mediation is recognized by reviewing the molecular defects such as the signal transduction $P_{sw}$ that control $A_{ppt}$. In this viewpoint, $P_{MPN} S_{Ed}$ comprising of $C^{CBT}_o$ and its derivatives have developed a new emphasis for $C^{NCR}_o$ drug discovery because of its durable ability to inhibit different types of $C^{NCR}_o$ $C^{CBT}_o$ and its byproducts inhibit $C^{NCR}_o$ development by a comprehensive variety of mechanisms ($M_{pret}$), comprising of pro- $A_{pret}$ installment of autophagy, $C^{EL}_o$ cycle seizure, inhibition of $C^{NCR}_o$ entrenchment and shifting $C^{CBT}_o$ also modifies numerous intracellular $S_{gls} P_{sw}$ [Figure 3]. $S_{gls}$ transducers and

### Table 1: List of minerals in $P_{MPN} S_{Ed}$

<table>
<thead>
<tr>
<th>Components</th>
<th>Nutrient value</th>
<th>% of RDA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na</td>
<td>7 mg</td>
<td>0.5</td>
</tr>
<tr>
<td>K</td>
<td>809 mg</td>
<td>17</td>
</tr>
<tr>
<td>Ca</td>
<td>46 mg</td>
<td>4.5</td>
</tr>
<tr>
<td>Cu</td>
<td>1.343 mg</td>
<td>159</td>
</tr>
<tr>
<td>Fe</td>
<td>8.82 mg</td>
<td>110</td>
</tr>
<tr>
<td>Mg</td>
<td>592 mg</td>
<td>148</td>
</tr>
<tr>
<td>Mn</td>
<td>4.543 mg</td>
<td>198</td>
</tr>
<tr>
<td>P</td>
<td>1.233 mg</td>
<td>176</td>
</tr>
<tr>
<td>Se</td>
<td>9.4$\mu$g</td>
<td>17</td>
</tr>
<tr>
<td>Zn</td>
<td>7.81 mg</td>
<td>71</td>
</tr>
</tbody>
</table>

### Table 2: List of $F_{TA}$ in $P_{MPN} S_{Ed}$

<table>
<thead>
<tr>
<th>Name</th>
<th>Structure</th>
<th>Content (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PA$^{A_d}$</td>
<td><img src="structure.png" alt="PA$^{A_d}$" /></td>
<td>10.68+/−0.42</td>
</tr>
<tr>
<td>Palmitoleic A$^{A_d}$</td>
<td><img src="structure.png" alt="Palmitoleic A$^{A_d}$" /></td>
<td>0.58+/−0.14</td>
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<tr>
<td>SA$^{A_d}$</td>
<td><img src="structure.png" alt="SA$^{A_d}$" /></td>
<td>8.67+/−0.27</td>
</tr>
<tr>
<td>OA$^{A_d}$</td>
<td><img src="structure.png" alt="OA$^{A_d}$" /></td>
<td>38.42+/−0.37</td>
</tr>
<tr>
<td>LA$^{A_d}$</td>
<td><img src="structure.png" alt="LA$^{A_d}$" /></td>
<td>39.84+/−0.08</td>
</tr>
<tr>
<td>L$_{5}$A$^{A_d}$</td>
<td><img src="structure.png" alt="L$_{5}$A$^{A_d}$" /></td>
<td>0.68+/−0.14</td>
</tr>
<tr>
<td>G$_{5}$A$^{A_d}$</td>
<td><img src="structure.png" alt="G$_{5}$A$^{A_d}$" /></td>
<td>1.14+/−0.00</td>
</tr>
<tr>
<td>Name</td>
<td>Category</td>
<td>Structure</td>
</tr>
<tr>
<td>------------------</td>
<td>----------</td>
<td>-----------</td>
</tr>
<tr>
<td>( L_{n}^{1} )</td>
<td></td>
<td><img src="image1" alt="Structure" /></td>
</tr>
<tr>
<td>( L_{n}^{1} ) epoxide</td>
<td></td>
<td><img src="image2" alt="Structure" /></td>
</tr>
<tr>
<td>15-cis- ( L_{n}^{1} )</td>
<td></td>
<td><img src="image3" alt="Structure" /></td>
</tr>
<tr>
<td>9(( \phi ))-cis- ( L_{n}^{1} )</td>
<td></td>
<td><img src="image4" alt="Structure" /></td>
</tr>
<tr>
<td>( \alpha )-carotene</td>
<td></td>
<td><img src="image5" alt="Structure" /></td>
</tr>
<tr>
<td>Viola ( X_{n}^{1} )</td>
<td></td>
<td><img src="image6" alt="Structure" /></td>
</tr>
<tr>
<td>Auro ( X_{n}^{1} )</td>
<td></td>
<td><img src="image7" alt="Structure" /></td>
</tr>
<tr>
<td>Flavo ( X_{n}^{1} )</td>
<td></td>
<td><img src="image8" alt="Structure" /></td>
</tr>
<tr>
<td>Luteo ( X_{n}^{1} )</td>
<td></td>
<td><img src="image9" alt="Structure" /></td>
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<tr>
<td>Chrysanthem ( X_{n}^{1} )</td>
<td></td>
<td><img src="image10" alt="Structure" /></td>
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<tr>
<td>( \alpha )-crypto ( X_{n}^{1} )</td>
<td></td>
<td><img src="image11" alt="Structure" /></td>
</tr>
<tr>
<td>Stigmasterol</td>
<td>Steroid</td>
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<tr>
<td>Squalene</td>
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<td><img src="image13" alt="Structure" /></td>
</tr>
<tr>
<td>Vicine</td>
<td>Alkaloid</td>
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<tr>
<td>Kuguacin</td>
<td></td>
<td><img src="image15" alt="Structure" /></td>
</tr>
<tr>
<td>( C_{ST} )</td>
<td></td>
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<tr>
<td>( C_{ST} ) A</td>
<td></td>
<td><img src="image17" alt="Structure" /></td>
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<tr>
<td>( C_{ST} ) B</td>
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activators of transcription ($T_R^{SC}$) 3 and Janus enzyme $S_{P_{tw}}$ $P_{tw}$ are the key M$_{AG}$ for $C_{CBT}$ to speak into necrobiosis to place forth their compelling malignant (M$_{AG}$) neoplasm impact. The capability of $C_{CBT}$ to prevail $C_{EL}$ cycling in the G2/M part by diversified controllers is additionally a major approach to fight different $C_{NCR}$ 32 $STAT3 (S_{P_{tw}}$) controls the exposition of genes (G$^*$) which intercede multiplication (e.g., c-myc and cyclin D1), lowers activities of pro-apoptotic G$^*$ (e.g., Bcl-xL, Bcl-2 and surviving) and/or accelerates maturation through vascular epithelial tissue protein (VEGF). Conversely, cytokines (C$_{tk}$) will inhibit the STAT-3 $S_{P_{tw}}$ $P_{tw}$. Protein empirical G$^*$, enacting the obliterator of C$_{tk}$ communication super molecule family, binding to JAK, represent the major negative regulators of the JAK/ $S_{P_{tw}}$ $S_{P_{tw}}$ $S_{P_{tw}}$. In recent past, it is accepted that $S_{P_{tw}}$ may also be called up by several alternative C$_{tk}$ like IL-7, IL-10, IL-20, leptin, WBC colony-stimulating issue and cuticular protein. 33 Admist the seven human STAT G$^*$, $S_{P_{tw}}$, a typical oncogenic communication $P_{tw}$ is integrally called up in many sorts of $C_{NCR}$ together with eighty-
two of glandular C_Arom^3 seventh of breast (B_R), C_NCR over eighty two of the C_Arom of the top and neck, seventy one of cavity M^35, neoplastic(N,^35) Dlaş^, over five hundred respiratory organ C_NCR and five hundredth of HCC, lymphomas and myelomas.^36 Uncontrolled doings of S^3 is unquestionable in an exceedingly form of t_R^m Cies, together with B_R M^AG, N,^35 Dlaş^, P_S^m C_NCR melanoma, multiple myeloma and C_NCR of the blood.35,36 Numerous G^n mutations cause organic activation of S^3, as for example over-phrasing and organic triggering of cuticular protein receptor (EGFR).37 S^3 takes part to t_R^m growth by widening the C_EL cycle by warding off necrobiosis and speculating onco G^n like e-Myc and Bcl-X. S^3 has lately been incontestable to enhance glandular C_Arom metastasis by nurturing P^S_R C_NCR exodus. C_CBT are identified as A^R, t_R^m agents associated with other M^3, like conflicting with S^3 S^R. They also influence the virtue of the actin cytoskeleton. As for instance, C_CBT E wards off the propagation of glandular C_Arom C_EL and disrupts the body architecture of simple protein and supplements.38 However, C_CBT A, B, E, I, impede the phosphorylation (P^S_R) of S^3 and/or C_JAK2 and same way rules out S^3 deoxyribonucleic A^'-attachment and S^3-mediated citron T_R^SC in C_Arom A549 line.39 Similarly, C_CBT I causes debasement of D_H R - S^3 in the B_R P^S_R and exocrine gland M^AG, N,^35 Dentiful^, C_EL lines (MDA-MB-231, MDA-MB-468 and Panc-1). Amazingly, C_CBT B and E are set out to persuade S^3_R in C_Arom C_EL lines (MDA-MB-231 and MCF-7).40 This study indicates that C_CBT exerts A^n - tumorigenic activity by selection of C_EL with activated S^3. In SAR consideration it is found that 5 C_CBT A, B, E, I and Q obstruct the actuation of S^3 and produce necrobiosis. In an exceeding mouse t_R^m heterograft model, C_CBT however did not suppress t_R^m growth. This indicates that JAK2 inhibition isn’t adequate to ward off tmR advancement suggesting thereby the power of C_CBT to impede t_R^m growth expounding its A^n - S^3 activity. These observations more legitimize S^3 as a drug exposition designing and supply proof that medical specialty assistants like C_CBT may judiciously cut back the P- S^3 levels in human C_EL. In distinction, K-Ras (R^S) mutations are found in thirty-five hundredths of primary large intestine C_NCR besides as in entrenched C_Arom C_EL lines. Thus, the company of oncogenic K- R^S, considerably shrivels the sensitivity of C_EL to dihydro C_CBT B, R and I presumably through K- R^S disagreement with S^3 arousal. Moreover, p53 and p21 shield C_EL from necrobiosis are lured by C_CBT. The similar studies ascertain that reactivity of human C_Arom C_EL to those 3 C_CBT falls back on the vicinity of oncogenic K- R^S and p53/p21 standing and establish that C_CBT exerts A^n - t_R^m genic activity within the absence of activated S^3.41

**Induction of A^pp**

C_CBT B, D, E, I and Ia influence A^pp in different classes of C_NCR C_EL by arresting the S^3 P^R_R, S^3 is a T_R^SC P^CT that rolls G^n expression via cross-talk with another T_R^SC P^CT, such as C^B (B^S), hypoxia-inducible factor-1, nuclear factor-B, c-myc, c-jun and closing off S^3 stimulation influenced A^pp. C_CBT B has distinct structural ups and downs as symbol for A^pp, which consists of nuclear fragmentation, chromatin contraction and embodiment of apoptotic bodies. C_CBT B may be significant for both inflicting the empathy of C_NCR C_EL to cytotoxic lymphocyte and inspiring A^n C_NCR immunity by the prohibition of the JAK2/ S^3 P^R_R. These M pinpoint that prohibition of the JAK/ S^3 P^R_R with C_CBT B may be impressive in C_NCR immunotherapy. Moreover, in human colon adenoc C_Arom the C_CBT B-influenced - A^pp is sustained by a reactive oxygen species system instead of that of S^3. C_CBT D stimulates the apoptotic P^R_R by annihilating S^3 activity in B_R C_NCR C_EL and splitting fragments to procaspase-3, procaspase-9 and PARP in human endometrial as well as ovarian C_NCR C_EL.42-45

**Induction of Autophagy**

C_CBT specifically C_CBT B and I, activate autophagosome development. They also initiate the gathering and changing over from light chain 3-1 to LC3II in several C_EL classes basically through inflection of production of mitochondrial-derived ROS and consequently activating ERK and JNK. Initiation is accomplished through the calling up of AMP-triggered protein kinase (K^N)/ mammalian target of p70S6K P^R_R instead of PI3K/Akt P^R_R.46

**Induction of Cell Cycle Arrest**

In human C_EL cycle changeover is organized by holoenzymes comprising of reciprocally regulatory and catalytic cyclin-dependent K^n, CDK (c^D), inhibitors like c^{D_k} 1, p21Waf1 and p27KIP1 perform as intrinsic controllers of C_EL cycle by hooking up to c^{D_k} complexes and lowering K^n activity.47 C_CBT persuades C_EL cycle blockage by reshaping different S^n P^R_R. C_CBT B brings about G2/M C_EL cycle apprehend in different C_NCR, such as, osteosarcoma C_EL non-small C_EL lung (E,^O), B R C_NCR glioblastoma multiform, cutaneous squamous C_EL, laryngeal squamous and pancreatic C_EL A_Arom^3.48-54

**Inhibition of C_NCR Invasion and Migration**

C_CBT B significantly destroys C_EL migration and invasion induced by impeding the P_H_R of Akt, p38 and ERK1/2 and the down-settlement of MMP-9. C_CBT E destroys
B_n^\text{C}_{\text{NCR}}^\text{M}_{\text{ch}}^\text{m} \text{ metastasis by distracting Arp/23-reliant actin polymerization and hindering the Src/FAK/Rac/JNK/MMP S_y^5 \text{ S}_{\text{edc}}^\text{m}^5 \text{ P}^\text{c}_\text{B}^\text{CBT} \text{ B management restrains cytokinin D_1, c-Myc and B_n^\text{a} \text{ view height, alteration to the nucleus of B_n^\text{a}^\text{a} \text{ and galectin-3. Summarized form of } A_n^\text{a} - \text{ C}_{\text{NCR}}^\text{M}_{\text{ch}}^\text{m} \text{ is shown in Figure 4.}

CONCLUSION

It may be concluded that due to phytochemical, pharmacological and nutritional values, C. pepo has attained high importance throughout the world. The available research data on C_{\text{CBT}}^\text{M}_{\text{CT}}\text{ indicate its } M_{\text{edc}} \text{ value especially for hyperplasia, } P^\text{a}_{\text{NCR}}^\text{m} \text{ C}_{\text{NCR}}^\text{M}_{\text{ch}}^\text{n} \text{ urinary D}_{\text{SEAS}}^\text{m} \text{ nephritis, bronchitis, hemorrhoid and anemia. The } M_{\text{edc}}^\text{m} \text{ properties of } C. \text{ pepo are due to the presence of different phytochemicals like Triterpene (T^\text{T}_{\text{m}}^\text{m}), alkaloid, cardiac G^\text{m}^\text{m}, etc. So, increasing } M_{\text{edc}}^\text{m} \text{ value of } C. \text{ pepo is demanding for the discovery of more potential phytochemicals which can lead to the improvement in drug formulation system. Pharmacological studies confirm the A_n^\text{a} \text{ bacterial, A_n^\text{a} \text{ viral, A_n^\text{a} \text{ ulcer and A_n^\text{a} \text{ t}}^\text{n} \text{ activities that provide scientific basis to the use of } C. \text{ pepo based on the traditional medicines but there is no report for formulation development. Different } C_{\text{CBT}}^\text{M}_{\text{CT}}\text{ compounds are also used to inhibit uncontrolled } C_{\text{EL}}^\text{m} \text{ division and induce } A_{\text{pp}}^\text{m} \text{ using plentiful } C_{\text{NCR}}^\text{M}_{\text{ch}}^\text{n} \text{ lines of human and t}_{\text{n}}^\text{n} \text{ xenografting of leukemia, lymphoma, B_n^\text{a}^\text{a}, P_n^\text{c}_\text{B}^\text{CBT}^\text{m}, L_{\text{c}}^\text{m}, os uterine cervix, liver, sk_{\text{N}}^\text{m}, colon, laryngeal, brain and pancreatic C_{\text{NCR}}^\text{M}_{\text{ch}}^\text{n} \text{ has also the capacity to prevent } P_{\text{H}_R}^\text{n} \text{ of } S_{\text{ta}}^\text{n}^3 \text{ and/or JAK2 and their consecutive invigoration play the sizable role in terms of mode of operation. C}_{\text{CBT}}^\text{M}_{\text{CT}}\text{ warrant eventual inquisitions exploring their exposition in uninvestigated origins and their offshoots for bettering the } A_n^\text{a} \text{ - } C_{\text{NCR}}^\text{M}_{\text{ch}}^\text{n} \text{ competence. Moreover, preclinical and clinical abstraction involving united regimen including } C_{\text{CBT}}^\text{M}_{\text{CT}}\text{ and standard chemo-immune- and/or radio-therapies should be programmed for future strategies.}

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CONFLICT OF INTEREST

Authors declare that there is no conflict of interest in this manuscript.

ABBREVIATIONS

A_{\text{c}}^\text{m} \text{ : Amino acids; A_{\text{n}}^\text{a} \text{ : Anti; Appt: Apoptosis; B_{\text{n}}^\text{m} \text{ : Breast; C}_{\text{NCR}}^\text{M}_{\text{ch}}^\text{n} \text{ : Cancer; C}_{\text{OSG}}^\text{M}_{\text{ch}}^\text{n} \text{ : Carcinogenesis; C}_{\text{Arom}}^\text{M}_{\text{ch}}^\text{n} \text{ : Carcinomas; C}_{\text{AR}}^\text{M}_{\text{ch}}^\text{n} \text{ : Carotenoids; c_{\text{L}}^\text{n} \text{ : CDK; C}_{\text{EL}}^\text{M}_{\text{ch}}^\text{n} \text{ : Cell; C}_{\text{CBT}}^\text{M}_{\text{CT}} \text{ : Cucurbita; C}_{\text{CBT}}^\text{M}_{\text{CT}} \text{ : Cucurbitacin; C}_{\text{ik}}^\text{M}_{\text{ch}}^\text{n} \text{ : Cytokines; D}_{\text{SEAS}}^\text{m} \text{ : Diseases; F}_{\text{CT}}^\text{m} \text{ : Factors; F}_{\text{TA}}^\text{m} \text{ : Fatty acids; F_{\text{n}}^\text{m} \text{ : Fruit; G}_{\text{K}}^\text{m} \text{ : Genes; G}_{\text{d}}^\text{m} \text{ : Glycosides; N}_{\text{K}}^\text{m} \text{ : Kinase; L}_{\text{CR}}^\text{M}_{\text{ch}} \text{ : Laricresinol; L A_{\text{c}}^\text{m} \text{ : Linoleic; L}_{\text{u}}^\text{m} \text{ : Lung; L}_{\text{n}}^\text{m} \text{ : Lutein; M}_{\text{NG}}^\text{m} \text{ : Malignant; M}_{\text{edc}}^\text{m} \text{ : Mechanisms; M}_{\text{edc}}^\text{m} \text{ : Medicinal; N}_{\text{L}}^\text{m}^\text{m} \text{ : Neoplastic; O}_{\text{A}}^\text{m} \text{ : Oleic acids; P A_{\text{d}}^\text{m} \text{ : Palmitic; P}_{\text{w}}^\text{m} \text{ : Pathway; P}_{\text{L}}^\text{m} \text{ : Plant; P_{\text{n}}^\text{m} \text{ : Prostate; P}_{\text{MPN}}^\text{m} \text{ : Pumpkin; R}_{\text{n}}^\text{m} \text{ : Ras; S}_{\text{L}}^\text{m} \text{ : Seed; S}_{\text{g}}^\text{m} \text{ : Signaling; S}_{\text{n}}^\text{m} \text{ : Skin; S}_{\text{CT}}^\text{m} \text{ : STAT3; S A_{\text{c}}^\text{m} \text{ : Stearic acids; T}_{\text{R}}^\text{m} \text{ : Transcription; T}_{\text{p}}^\text{m} \text{ : Triterpene; t}_{\text{n}}^\text{n} \text{ : Tumor; X}_{\text{t}}^\text{m} \text{ : Xanthine.}

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SUMMARY

- Pumpkin seed contains cucurbitacin and its derivatives
- They are anti-proliferative agents
- These are blocked by JAK/STAT signaling pathway
- Blocking by JAK/STAT signaling pathway may involve several mechanisms such as induction of autophagy, induction of cell cycle arrest, induction of apoptosis, and inhibition of cancer Invasion and migration.

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